## Everything you need to know about managing in axSpA

### POS0244 PROTOCOL VIOLATION IN A TREAT-TO-TARGET STRATEGY IN AXIAL SPONDYLOARTHRITIS: DATA FROM THE OPEN-LABEL, PRAGMATIC, CLUSTER-RANDOMISED TICOSPA TRIAL

**Keywords:** Randomized control trial, Treat to target, Spondyloarthritis

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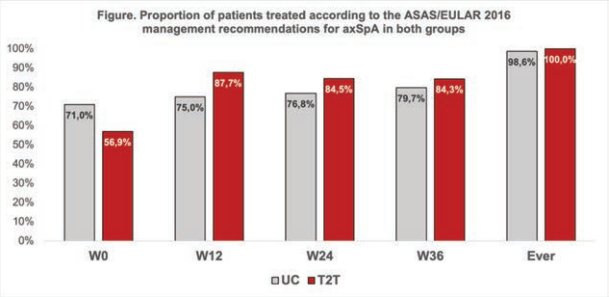
**Background:** Despite the ASAS-HI (primary outcome) did not reach statistical significance in the TICOSPA trial, other clinically relevant secondary outcomes were numerically higher in the treat-to-target (T2T) strategy in comparison to Usual Care (UC), including the ASAS-HI. Three hypotheses have been considered to explain this observation: a lack of power, the risk of protocol violations in the T2T arm and the potential optimal care in the UC arm.
**Objectives:** a) To evaluate the proportion of patients (pts) with protocol violations in the T2T group during the 48 weeks (48W) of follow up as well as the impact and predictive factors of such violation; b) to compare the proportion of pts treated according to the ASAS/EULAR 2016 management recommendations for axSpA over the follow-up period in both arms.
**Methods:** *Study design:* pragmatic, prospective, cluster-randomized controlled, 48W trial (NCT03043846) with 18 participating centers. *Inclusion criteria*: Pts with a diagnosis of axSpA and fulfilling ASAS criteria, non-optimally treated with NSAIDs, bDMARD-naïve and ASDAS >2.1. *Study treatment regimens:* SpA expert centers were selected to participate in the study: then, they were randomly allocated (1:1) to the treatment arm: a) T2T: the management strategy was pre-specified based on strict application of 2016 ASAS/EULAR axSpA recommendations (Q4W), with a target of ASDAS <2.1; b) UC: treatment decisions at the rheumatologist's discretion (Q12W). *Statistical analysis*: *a) Protocol violations:* in the T2T arm were evaluated at every visit by the question "Was the recommendation for treatment from last visit followed by physician and patient?". Factors associated with at least one protocol violation over the study were evaluated using multivariate logistic regression. Outcomes at 48W were compared between T2T violators (T2T-V) vs. T2T non-violators (T2T-NV) vs. UC using ANOVA test; b) *optimal care in UC:* proportion of pts treated according to the 2016 ASAS/EULAR recommendations over the follow-up period in both arms were compared.
**Results:** 160 pts initiated the trial (T2T:80 and UC:80). *a) Protocol violations:* In the T2T arm, 41/80 (51.2%) pts violated the protocol during at least one visit. A total of 27.7% violations were represented by a lack of switching to a second NSAID and 41.2% by a lack of initiation of a first bDMARD. Baseline predictive factors independently associated with the protocol violation were the country (France vs. others; OR 3.8 (95%CI 1.1-15.0)), female sex (OR 4.4 (1.5-15.1)), diagnosis delay ≤7 years (OR 3.4 (1.1-11.9)), HLA-B27 negative (OR 6.4 (1.6-32.2)) and CRP≥6mg/L (OR 4.2 (1.3-15.9)). After 48W of follow-up, T2T-NV vs. T2T-V showed similar ratios of ASAS-HI improvement. ASDAS-LDA, ASDAS-ID and ASDAS-CII outcomes were more prevalent in T2T-NV vs. T2T-V, although these differences did not reach statistical significance (Table 1). b) *Optimal care in UC*: the proportion of pts managed according to the 2016 ASAS/EULAR recommendations was very high in both arms, i.e. always above 75% also in the UC arm, although no statistical differences were found (p=0.490) (Figure 1).

**Table 1. Impact of protocol violation across groups**

| | Groups | | | p-value | | | |
|---|---|---|---|---|---|---|---|
| | T2T-NV N = 39 | T2T-V N = 41 | UC N = 80 | ANOVA | T2T-NV vs. T2T-V | T2T-NV vs. UC | T2T-V vs. UC |
| **ASAS40 W48** | 14 (35.9%) | 16 (39.0%) | 19 (24.1%) | 0.177 | 0.773 | 0.177 | 0.087 |
| **ASDAS-LDA W48** | 24 (61.5%) | 19 (46.3%) | 32 (40.5%) | 0.087 | 0.173 | **0.027** | 0.504 |
| **ASDAS-ID W48** | 11 (28.2%) | 8 (19.5%) | 10 (12.7%) | 0.117 | 0.361 | **0.038** | 0.319 |
| **ASDAS-CII W48** | 22 (56.4%) | 16 (39.0%) | 26 (32.9%) | **0.049** | 0.120 | **0.015** | 0.506 |
| **ASDAS-MI W48** | 6 (15.4%) | 8 (19.5%) | 9 (11.4%) | 0.479 | 0.627 | 0.565 | 0.226 |
| **ASAS-HI improvement W48** | 14 (35.9%) | 16 (39.0%) | 21 (26.6%) | 0.322 | 0.773 | 0.297 | 0.162 |

**Conclusion:** The prevalence of pts violating the protocol in the T2T arm was high, although it did not explain the non-significance of the primary outcome in the TICOSPA trial (ASAS-HI improvement). In contrast, the proportion of pts managed according to the ASAS/EULAR recommendations in the UC arm was very high, suggesting that the UC group was optimally treated.

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### POS0245 BLOOD-BASED EXTRACELLULAR MATRIX BIOMARKERS CAN IDENTIFY ENDOTYPES OF PATIENTS WITH AXSPA AND RESPONDERS TO ADALIMUMAB TREATMENT

**Keywords:** Spondyloarthritis, Biomarkers

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**Background:** Axial spondyloarthritis (axSpA) is a chronic inflammatory disease associated with extracellular matrix (ECM) remodelling of the cartilage, bone, and connective tissues. Adalimumab (ADA) is an effective treatment, but not all patients respond, and this may relate to subtypes of the disease (endotypes). Serological quantification of ECM-mediated biomarkers may be useful to identify axSpA endotypes and monitor treatment response to ADA.
**Objectives:** 1) To identify endotypes of patients with axSpA using blood-based ECM biomarkers at baseline and 2) To investigate differences in response to ADA by BASDAI and ASDAS criteria within the endotypes.
**Methods:** ECM biomarkers were measured in serum from patients with axSpA in the three studies (MASH (n=41), DANISH (n=49) and ASIM (n= 45)) at baseline [1–3]. MASH was a cross-sectional study while in DANISH and ASIM patients were randomised to receive treatment with ADA 40 mg or placebo every other week (e.o.w.) for 6 or 12 weeks (ASIM and DANISH, respectively) followed by ADA 40 mg e.o.w. for an additional 18 or 12 weeks (ASIM and DANISH, respectively). Biomarkers of type II collagen formation (PRO-C2), type I collagen degradation (C1M), inflammation (CRP, CRPM) citrullinated and degraded vimentin (VICM) and neutrophil activity (CPa9-HNE) were measured by immunoassays. Biomarker data was log-transformed, standardized by mean centering and scaled by the standard deviation prior to principal component analysis (PCA) and K-means clustering. Response to ADA based on BASDAI50 response, ASDAS clinical important improvement (CII) and major improvement (MI) at study week 24 was compared in the PCA components and between clusters using Mann-Whitney tests. Key demographic parameters were also compared between clusters using Mann-Whitney and chi-squared tests.
**Results:** The variability of baseline ECM biomarker data among patients with axSpA was mainly explained by two dimensions (PC1 and PC2). Type I collagen degradation and inflammation biomarkers (C1M and CRP), reflecting tissue inflammation, were the primary contributors to PC1, whereas type II collagen formation (PRO-C2), reflecting cartilage turnover, contributed the most to PC2 (Figure 1A). In ADA-treated patients, BASDAI50 responders, patients with